Index No. 7/12/Life Sc./21

ABSTRACT

Title : **'Understanding Extracellular Matrix Remodelling in Rheumatic Heart Valve for Biomarker Identification.'**

Submitted by : **TANIMA BANERJEE**

Background: In rheumatic heart disease (RHD) heart valves are damaged by the rheumatic fever which carry a significant burden in developing countries as well as indigenous populations within developed countries. It is primarily a hypersensitive reaction to streptococcal antigens. In RHD, mitral valve gets affected. Thickening and fibrosis occurs in affected mitral valve. Human Valve is mainly composed of fibroblast from where collagens are known to be synthesized. During the biosynthesis of procollagen to triple helical monomers, procollagen C- terminal propeptide (PICP) is cleaved and released into the circulating blood. Thus, PICP is found to be an important marker for collagen synthesis. To date, no such biomarkers of rheumatic heart disease were identified.

Observations: This study included the subjects with RHD before and after valve replacement surgery and age and sex matched controls in Indian subpopulation. Management involves periodic clinical monitoring with echocardiography. Circulating levels of markers of collagen turnover were monitored by immunoassay. Histopathology studies were performed on excised mitral valve leaflets. A p value <0.05 was considered statistically significant. Plasma level of C terminal propeptide of type I collagen (PICP) in RHD subjects (n=78) was 400% higher than in controls ($P<0.0001$). Receiver operating characteristic curve analysis was performed to establish PICP as a better marker (AUC = 0.95; 95% CI = 0.91 - 0.99; $p<0.0001$). A cut-off > 459 ng /mL for PICP provided 91% sensitivity, 90% specificity and a likelihood ratio of 9 in diagnosing

RHD. Valve pathophysiology included inflammation, neovascularisation and extensive leaflet fibrosis.

Conclusions: The fibrotic state of the rheumatic valve correlated with remarkable elevation of plasma PICP level which precedes the occurrence of myocardial dysfunction and overt heart disease. Thus, an antifibrotic agent might be useful for therapeutic intervention of RHD.

Key Words: Fibrosis, Mitral valve, Mitral stenosis, Mitral regurgitation, PICP , Neovascularisation.

Tanima Banerjee
(TANIMA BANERJEE)

Dated : 21/12/2016

Signature with Seal of the Supervisor

Dated : 21/12/2016

अरुण बंद्योपाध्याय/ ARUN BANDYOPADHYAY
वरिष्ठ प्रधान वैज्ञानिक, प्रोफेसर (एसीएसआईआर)
Senior Principal Scientist, Professor (AcSIR)
प्रमुख, कोशिका जीवविज्ञान और शरीर विज्ञान/ Head, Cell Biology and Physiology Division
सीएसआईआर -भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR- INDIAN INSTITUTE OF CHEMICAL BIOLOGY
4,राजा एस. सी. मल्लिक रोड / Raja S. C. Mullick Road
कोलकाता, भारत / Kolkata - 700 032, India